

# Patterns and Intensity of Medical Therapy in Patients Undergoing Percutaneous Coronary Intervention

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**A**LTHOUGH PERCUTANEOUS coronary intervention (PCI) may improve outcomes for patients with acute coronary syndrome, optimal medical therapy (OMT) results in similar rates of cardiovascular events when compared with PCI in patients with stable coronary artery disease (CAD).<sup>1,2</sup> In fact, a meta-analysis of 11 trials<sup>2</sup> concluded that there was no benefit of PCI in preventing myocardial infarction or death in patients with stable CAD. The most definitive randomized trial comparing the effectiveness of OMT vs OMT plus PCI in patients with stable CAD was the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) study.<sup>3</sup> In the COURAGE trial, patients with stable CAD underwent diagnostic coronary angiography to define their coronary anatomy and received aggressive secondary prevention therapy,<sup>4</sup> with half of the patients also being randomized to upfront PCI. Because PCI did not improve survival or prevent myocardial infarctions in the COURAGE trial,<sup>3,5</sup> current guidelines supporting the aggressive use of OMT before revascular-

**Context** The Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) study, which provided optimal medical therapy (OMT) to all patients and demonstrated no incremental advantage of percutaneous coronary intervention (PCI) on outcomes other than angina-related quality of life in stable coronary artery disease (CAD), suggests that a trial of OMT is warranted before PCI. It is unknown to what degree OMT is applied before PCI in routine practice or whether its use increased after the COURAGE trial.

**Objective** To examine the use of OMT in patients with stable angina undergoing PCI before and after the publication of the COURAGE trial.

**Design, Setting, and Participants** An observational study of patients with stable CAD undergoing PCI in the National Cardiovascular Data Registry between September 1, 2005, and June 30, 2009. Analysis compared use of OMT, both before PCI and at the time of discharge, before and after the publication of the COURAGE trial. Optimal medical therapy was defined as either being prescribed or having a documented contraindication to all medicines (antiplatelet agent,  $\beta$ -blocker, and statin).

**Main Outcome Measures** Rates of OMT before PCI and at discharge (following PCI) between the 2 study periods.

**Results** Among all 467 211 patients (173 416 before [37.1%] and 293 795 after [62.9%] the COURAGE trial) meeting study criteria, OMT was used in 206 569 patients (44.2%; 95% confidence interval [CI], 44.1%-44.4%) before PCI and in 303 864 patients (65.0%; 95% CI, 64.9%-65.2%) at discharge following PCI ( $P < .001$ ). Before PCI, OMT was applied in 75 381 patients (43.5%; 95% CI, 43.2%-43.7%) before the COURAGE trial and in 131 188 patients (44.7%; 95% CI, 44.5%-44.8%) after the COURAGE trial ( $P < .001$ ). The use of OMT at discharge following PCI before and after the COURAGE trial was 63.5% (95% CI, 63.3%-63.7%) and 66.0% (95% CI, 65.8%-66.1%), respectively ( $P < .001$ ).

**Conclusion** Among patients with stable CAD undergoing PCI, less than half were receiving OMT before PCI and approximately two-thirds were receiving OMT at discharge following PCI, with relatively little change in these practice patterns after publication of the COURAGE trial.

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ization are logically rational so that the need for additional treatment with PCI to control symptoms can be assessed.<sup>6,7</sup>

Although suboptimal translation of important clinical findings to routine clinical care has been previously documented,<sup>8-12</sup> including in patients with CAD,<sup>13</sup> this has never been shown in the setting of PCI, a common and costly procedure.<sup>8</sup> Furthermore, the effect of widely publicized clinical trials, such as the COURAGE trial,<sup>14</sup> has not been examined.

We therefore sought to describe current practice patterns surrounding the use of OMT before and after PCI and to examine whether the use of OMT changed after the publication of the COURAGE trial. By conducting this analysis in the largest PCI registry in the United States to our knowledge, we sought to describe whether clinical practice appeared to reflect adoption of clinical trial evidence and illuminate opportunities to improve patient care.

## METHODS

### Data Source

Within the National Cardiovascular Data Registry, we analyzed data from the CathPCI Registry, which is cosponsored by the American College of Cardiology and the Society for Cardiovascular Angiography and Interventions. The CathPCI Registry is a national registry of hospitals in the United States and has been previously described.<sup>15-18</sup>

In brief, cardiac catheterization laboratories submit data on consecutive patients receiving PCI according to rigorous data quality assurance standards, including data completeness and validity checks upon entry, and periodic site audits. In return for submitting data, institutions receive performance reports that aid quality improvement efforts.

Demographic and clinical data including admission symptoms, cardiovascular risk factors, medications on admission to and in the catheterization laboratory, and medications on discharge from the hospital are collected. In addition, the National Cardiovascu-

lar Data Registry contains detailed technical data regarding the catheterization procedure, the angiographic findings, and the coronary interventions performed. Specifically, we examined changes in the use of OMT before PCI and at the time of discharge, both before and after the publication of the COURAGE trial.

Because this research involved analysis of an existing database without the use of patient identification, the Weill Cornell Medical College institutional review board authorized an exemption. Race/ethnicity was classified from retrospective chart review at each institution with options defined by the National Cardiovascular Data Registry to assess for differences in care patterns between racial and ethnic groups.

### Study Population

We analyzed data from 2 study periods surrounding the March 26, 2007, release of the COURAGE trial results (19 months before the COURAGE trial [September 1, 2005-March 25, 2007] and 24 months after the COURAGE trial [July 1, 2007-June 30, 2009]). A 3-month period after the release of the COURAGE trial was excluded to allow for dissemination of the study's results. In these periods, we identified patients without acute coronary syndrome presenting for elective PCI. Similar to, although less restrictive than, the entry criteria from the COURAGE trial, our analysis excluded patients with cardiogenic shock, left main CAD of 50% or more without prior coronary artery bypass graft (CABG) surgery, and a left ventricular ejection fraction of 30% or less.

We then restricted the analyses for 2 sensitivity analyses. First, we conducted an analysis that approximated the COURAGE entry criteria even more closely by also excluding patients without a lesion of at least 70% and a positive stress test, or without a lesion of at least 80% and symptoms, and with prior PCI or CABG surgery in the 6 months before the index procedure. Second, we performed an analysis limiting the study population to only those

patients with known cardiovascular disease (documented history of prior myocardial infarction, PCI, CABG surgery, peripheral artery disease, cardiovascular disease, or a diagnosis of stable angina) before the PCI so as to identify patients whose coronary disease was not newly diagnosed at the time of PCI.

### Definitions of OMT

Similar analytic strategies were used in both study periods. The primary end points were the rates of OMT before and after PCI between the 2 study periods. Both before and after PCI OMT were defined similarly as patients being prescribed aspirin (or thienopyridine if after PCI),  $\beta$ -blocker, and a statin, or having contraindications to these therapies. To be categorized as receiving OMT, individual patients must have been either prescribed or had reported contraindications to all medications in each category. For example, if a patient before PCI was taking an aspirin and a  $\beta$ -blocker and had a documented contraindication to a statin, that patient would be categorized as meeting OMT. If a patient did not meet all elements for OMT, through either being prescribed or by having a documented contraindication, then that patient was classified as not receiving OMT.

The composite OMT percentages, both before and after PCI, were calculated using the number of patients receiving OMT, as defined above, as the numerator and the total number of patients receiving PCI as the denominator. Data on the use of angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs) were recorded at discharge and could be used to calculate their use among those patients in whom they were clinically indicated. Therefore, in keeping with the COURAGE definition of OMT for patients with documented CAD, which encouraged an ACE inhibitor or ARB for all patients,<sup>4</sup> and given that the guidelines for chronic stable ischemic heart disease also recommend an ACE inhibitor or ARB for important subgroups of patients,<sup>19</sup> we also examined OMT af-

ter PCI, defined as patients being prescribed aspirin or thienopyridine,  $\beta$ -blocker, statin, and ACE inhibitor or ARB, if indicated by an ejection fraction of less than 40%, hypertension, diabetes, chronic kidney disease, or glomerular filtration rate by the Modification of Diet in Renal Disease equation of less than 60 mL/min/1.73 m<sup>2</sup>. Secondary end points included the rates of individual medications.

### Statistical Analysis

Categorical variables were compared using Pearson  $\chi^2$  tests and continuous or ordinal variables were compared using Wilcoxon rank sum tests. A time-series analysis was generated demonstrating rates of OMT by procedure month before and after the release of the COURAGE trial results. McNemar test was used to compare before and after PCI medical therapy use. Patients who died during catheterization and

those missing OMT data (<0.4% of records) were excluded. All statistical tests were 2-sided, with  $P < .05$  defined as the level of significance. All analyses were performed using SAS version 9.2 (SAS Institute, Cary, North Carolina).

### RESULTS

The initial CathPCI Registry population in the study period included 1 680 753 PCI procedures. After excluding 1 198 842 patients (71.3%) who did not have elective PCI for stable CAD, 12 990 patients (0.8%) who did not meet the COURAGE trial entry criteria, and 1710 patients (0.1% of total population, 0.4% of study population) who died or had missing data, the final study population included 467 211 patients (27.8% of the total CathPCI Registry data set in the study period). Rates of patients with missing data and deaths were similar between the 2 periods.

A total of 1013 hospitals participated in the CathPCI Registry during the study, one of which was excluded due to missing data. The hospitals had a mean of 458 beds, were mostly urban (60.3%), were mostly private or community hospitals (87.4%), and approximately half were teaching hospitals (51.6%). The median (interquartile range) annual PCI volume in the hospitals was 875 (548-1478) cases.

A total of 467 211 patients receiving PCI procedures were included in the analysis, with 173 416 patients (37.1%) and 293 795 patients (62.9%) in the before and after COURAGE periods, respectively. The mean number of patients per month in the study was 10 865 (range, 6824-14 473 patients). In general, patients who were receiving OMT before their PCI had more comorbidities and prior cardiovascular disease compared with patients who

**Table 1.** Demographic and Clinical Characteristics of the Study Population<sup>a</sup>

Characteristics	No. (%) of Patients		
	Total (N = 467 211)	Receiving OMT Before PCI (n = 206 569)	Not Receiving OMT Before PCI (n = 260 642)
Age, mean (SD), y	65.6 (11.1)	65.3 (11.0)	65.8 (11.1)
Male sex	316 943 (67.8)	142 957 (69.2)	173 986 (66.8)
White race	390 885 (83.7)	174 145 (84.3)	216 740 (83.2)
Presenting with symptoms	307 507 (65.8)	137 075 (66.4)	170 432 (65.4)
Hypertension	384 628 (82.3)	178 762 (86.5)	205 866 (79.0)
Dyslipidemia	383 632 (82.1)	188 129 (91.1)	195 503 (75.0)
BMI $\geq 30$	207 285 (44.4)	94 486 (45.7)	112 799 (43.3)
Previous PCI	205 460 (44.0)	113 789 (55.1)	91 671 (35.2)
Diabetes	166 830 (35.7)	77 006 (37.3)	89 824 (34.5)
Previous myocardial infarction ( $>7$ d)	129 636 (27.8)	74 031 (35.8)	55 605 (21.3)
Family history of CAD	120 566 (25.8)	54 419 (26.3)	66 147 (25.4)
Previous CABG surgery	91 903 (19.7)	50 558 (24.5)	41 345 (15.9)
Current tobacco use	85 457 (18.3)	36 024 (17.4)	49 433 (19.0)
Chronic lung disease	69 605 (14.9)	28 704 (13.9)	40 901 (15.7)
Peripheral vascular disease	60 636 (13.0)	28 353 (13.7)	32 283 (12.4)
Cerebrovascular disease	53 268 (11.4)	24 826 (12.0)	28 442 (10.9)
Previous heart failure	43 804 (9.4)	21 460 (10.4)	22 344 (8.6)
Previous renal failure	23 291 (5.0)	10 906 (5.3)	12 385 (4.8)
Postprocedure length of stay, median (5th-95th percentile), d	2 (2-4)	2 (2-4)	2 (2-4)
Postprocedure discharged to home	461 393 (98.8)	204 270 (98.9)	257 123 (98.7)
Government insurance	255 987 (54.8)	110 721 (53.6)	145 266 (55.7)
Uninsured	8675 (1.9)	4003 (1.9)	4672 (1.8)

Abbreviations: BMI, body mass index calculated as weight in kilograms divided by height in meters squared; CABG, coronary artery bypass graft; CAD, coronary artery disease; OMT, optimal medical therapy; PCI, percutaneous coronary intervention.

<sup>a</sup> $P < .001$  for all comparisons of patients receiving OMT and not receiving OMT before PCI.

were not receiving OMT before their procedure (TABLE 1).

Patients in the before and after COURAGE trial periods were similar in demographic and clinical characteristics, with approximately one-third of patients being asymptomatic in both study periods (eTable 1, available at <http://www.jama.com>). Throughout the entire study period, physicians used the opportunity of performing PCI to improve patients' medical regimens, with 206 569 patients (44.2%; 95% confidence interval [CI], 44.1%-44.4%) receiving OMT before PCI and 303 864 patients (65.0%; 95% CI, 64.9%-65.2%) receiving OMT at the time of discharge ( $P < .001$ ) (TABLE 2). When analyzing only those patients with known cardiovascular disease, the patterns were similar, although the rates of OMT were slightly higher (79 539 [53.6%; 95% CI, 53.3%-53.8%] and 104 366 [70.3%; 95% CI, 70.1%-70.6%], respectively;  $P < .001$ ) (Table 2).

#### Use of OMT Prior to PCI Before and After the COURAGE Trial

Before the COURAGE trial, the rate of OMT at the time of PCI was 43.5% (95% CI, 43.2%-43.7%;  $n = 75\,381$ ) (TABLE 3). Although the increase in the proportion of patients receiving OMT before PCI after the COURAGE trial was statistically significantly higher, it was of little clinical significance (131 188 patients [44.7%; 95% CI, 44.5%-44.8%];  $P < .001$  for difference between the 2 periods). The rates of OMT before PCI in each study period month showed a small increase during the 46 months of observation, with an OMT rate before PCI of 43.4% in September 2005 and an OMT rate after PCI of 45.0% in June 2009 (eTable 2). There was no noticeable increase in OMT rates before PCI in the period immediately after the March 2007 release of the COURAGE trial (FIGURE). The OMT rate before PCI was 43.9% in March 2007, before the trial results were known, followed after the publication by OMT rates before PCI of 44.1%, 43.7%, and 43.1% in July,

August, and September 2007, respectively (eTable 2). The rates of the individual medications, with the exception of aspirin before PCI as part of OMT, increased over time, although the absolute increases were small (Table 3).

#### Use of OMT Following PCI Before and After the COURAGE Trial

The overall rate of OMT (aspirin or thienopyridine,  $\beta$ -blocker, and statin) after PCI, a time at which the diagnosis of significant obstructive

**Table 2.** Medication Prescription Rates for Patients Before and After PCI<sup>a</sup>

Individual Medications	No. (%) [95% CI] of Patients	
	Before PCI	After PCI
<b>All Patients (N=467 211)</b>		
OMT <sup>b</sup>	206 569 (44.2) [44.1-44.4]	303 864 (65.0) [64.9-65.2]
Antiplatelet agent <sup>c</sup>	413 391 (88.5) [88.4-88.6]	463 205 (99.2) [99.1-99.2]
$\beta$ -Blocker	292 532 (62.6) [62.5-62.8]	351 207 (75.2) [75.1-75.3]
Statin	293 095 (62.8) [62.6-62.9]	391 966 (83.9) [83.8-84.0]
<b>Patients With Prior Diagnosis of CVD (n=148 423)</b>		
OMT <sup>b</sup>	79 539 (53.6) [53.3-53.8]	104 366 (70.3) [70.1-70.6]
Antiplatelet agent <sup>c</sup>	135 200 (91.1) [91.0-91.3]	147 573 (99.4) [99.4-99.5]
$\beta$ -Blocker	103 862 (70.0) [69.8-70.2]	118 174 (79.6) [79.4-79.9]
Statin	104 319 (70.3) [70.1-70.1]	128 073 (86.3) [86.2-86.5]
<b>Patients With No Prior Diagnosis of CVD (n=318 788)</b>		
OMT <sup>b</sup>	127 030 (39.9) [39.7-40.0]	199 498 (62.6) [62.4-62.8]
Antiplatelet agent <sup>c</sup>	278 191 (87.3) [87.2-87.4]	315 632 (99.0) [99.0-99.1]
$\beta$ -Blocker	188 670 (59.2) [59.0-59.4]	233 033 (73.1) [73.0-73.3]
Statin	188 776 (59.3) [59.1-59.4]	263 893 (82.8) [82.7-83.0]

Abbreviations: CI, confidence interval; CVD, cardiovascular disease; OMT, optimal medical therapy; PCI, percutaneous coronary intervention.

<sup>a</sup> $P < .001$  for all comparisons of before PCI and after PCI. Individual medications are defined as either being prescribed a medication or having a documented contraindication.

<sup>b</sup>Defined as either being prescribed, or having a documented contraindication, to all medicines (antiplatelet agent,  $\beta$ -blocker, and statin).

<sup>c</sup>Antiplatelet is defined as aspirin for before PCI and as aspirin or thienopyridine for after PCI.

**Table 3.** Medication Prescription Rates for Patients Before and After PCI and Before and After the COURAGE Trial Period<sup>a</sup>

Individual Medications	Total No. (%) of Patients (N = 467 211)	No. (%) [95% CI] of Patients	
		Before COURAGE (n = 173 416)	After COURAGE (n = 293 795)
Before PCI			
OMT <sup>b</sup>	206 569 (44.2)	75 381 (43.5) [43.2-43.7]	131 188 (44.7) [44.5-44.8]
Antiplatelet agent <sup>c</sup>	413 391 (88.5)	153 967 (88.8) [88.6-88.9]	259 424 (88.3) [88.2-88.4]
β-Blocker	292 555 (62.6)	107 371 (62.0) [61.7-62.2]	185 184 (63.1) [62.9-63.2]
Statin	293 137 (62.7)	108 166 (62.4) [62.2-62.6]	184 971 (63.0) [62.8-63.2]
After PCI			
OMT <sup>b</sup>	303 864 (65.0)	110 085 (63.5) [63.3-63.7]	193 779 (66.0) [65.8-66.1]
Antiplatelet agent <sup>c</sup>	463 257 (99.2)	171 716 (99.0) [99.0-99.1]	291 541 (99.2) [99.2-99.3]
β-Blocker	351 280 (75.2)	128 375 (74.0) [73.8-74.2]	222 905 (75.9) [75.7-76.0]
ACE inhibitor or ARB <sup>d</sup>	278 274 (59.6)	100 025 (57.7) [57.4-57.9]	178 249 (60.7) [60.5-60.9]
Statin	392 101 (84.0)	143 427 (82.7) [82.6-82.9]	248 674 (84.7) [84.6-84.8]

Abbreviations: ACE, angiotensin-converting enzyme; ARB, angiotensin II receptor blocker; CI, confidence interval; COURAGE, Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation; OMT, optimal medical therapy; PCI, percutaneous coronary intervention.

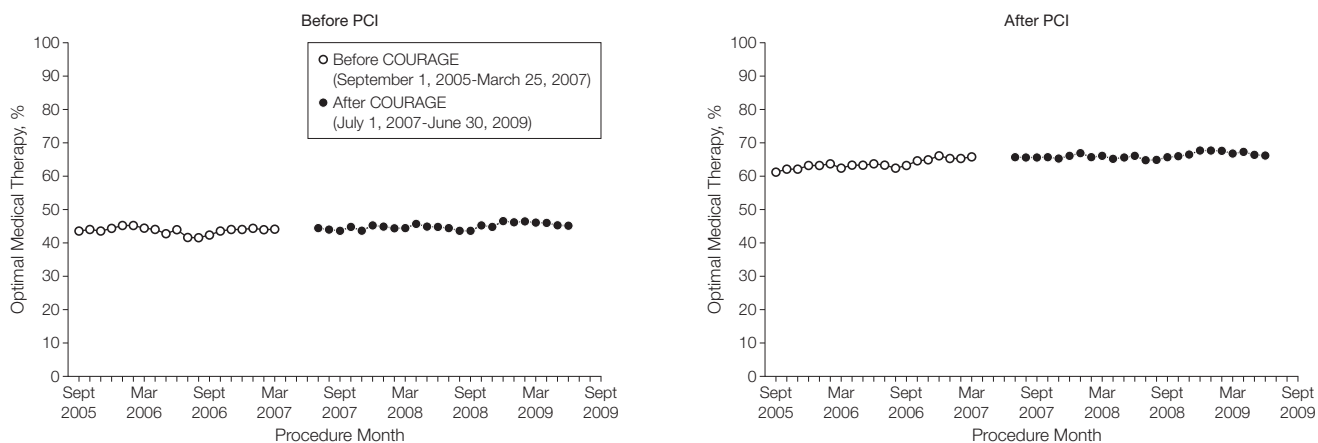
<sup>a</sup> $P < .001$  for all comparisons of before and after the COURAGE trial. The COURAGE trial was published on March 26, 2007 (September 1, 2005-March 25, 2007, for before the COURAGE trial and July 1, 2007-June 30, 2009, for after the COURAGE trial). Individual medications are defined as either being prescribed a medication or having a documented contraindication.

<sup>b</sup>Defined as either being prescribed, or having a documented contraindication, to all medicines (antiplatelet agent,  $\beta$ -blocker, and statin).

<sup>c</sup>Antiplatelet is defined as aspirin prescribed in patients before PCI and as aspirin or thienopyridine prescribed in patients after PCI.

<sup>d</sup>If applicable.



**Figure.** Percentage of Patients Achieving Optimal Medical Therapy Before and After PCI by Procedural Month

PCI indicates percutaneous coronary intervention; COURAGE, Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation. The COURAGE trial was published on March 26, 2007. Optimal medical therapy was defined as either being prescribed or having a documented contraindication to all medicines (antiplatelet agent,  $\beta$ -blocker, and statin).

CAD had been confirmed, before the COURAGE trial was 63.5% (95% CI, 63.3%-63.7%;  $n = 110\,085$ ) and increased to 66.0% (95% CI, 65.8%-66.1%;  $n = 193\,779$ ) after the COURAGE trial ( $P < .001$ ) (Table 3). The time-series analysis of OMT use after PCI also showed no noticeable increase in the months after the COURAGE trial publication (Figure).

Using the OMT definition for patients after PCI of aspirin or thienopyridine,  $\beta$ -blockers, statin, and ACE inhibitor or ARB for eligible patients ( $n = 413\,470$  [88.5% of total population]), the rates of OMT in patients were 43.4% (95% CI, 43.2%-43.6%;  $n = 75\,247$ ) and 45.9% (95% CI, 45.7%-46.1%;  $n = 134\,843$ ) before and after the COURAGE trial, respectively ( $P < .001$  for difference between the periods). The rates of the individual components of this secondary prevention also increased slightly over time (Table 3). Of all the secondary prevention medications after PCI, only the aspirin or thienopyridine was applied to a high degree in 171 716 patients (99.0%; 95% CI, 99.0%-99.1%) and 291 541 patients (99.2%; 95% CI, 99.2%-99.3%) before and after the COURAGE trial, respectively ( $P < .001$ ).

### Sensitivity Analyses

A sensitivity analysis restricted to the population of patients more closely meeting the inclusion and exclusion criteria of the COURAGE trial (265 184 total patients; 98 565 and 166 619 patients before and after the COURAGE trial, respectively) did not substantially alter the estimates of OMT use before PCI (before PCI OMT rate before the COURAGE trial was 40.0% [95% CI, 39.7%-40.3%] and after the COURAGE trial was 41.1% [95% CI, 40.9%-41.4%;  $P < .001$  for difference between the periods]). Similarly, minimal changes in the use of OMT after treatment were observed (61.8%; 95% CI, 61.5%-62.1% before COURAGE trial vs 64.3%; 95% CI, 64.1%-64.5% after COURAGE trial;  $P < .001$  for difference between the periods).

A second sensitivity analysis was restricted to those patients with known cardiovascular disease before PCI (148 423 patients [31.8%], with 55 494 [32.0%] before the COURAGE trial and 92 929 [31.6%] after the COURAGE trial). This analysis demonstrated higher rates of OMT before the procedure than in the main study population, but little change following the COURAGE trial (before PCI: OMT rates were 53.5% [95% CI, 53.0%-53.9%] and

53.7% [95% CI, 53.3%-54.0%] before and after the COURAGE trial, respectively;  $P = .44$  for difference between the periods). The use of OMT after PCI also showed a similar pattern (after PCI: OMT rates were 68.6% [95% CI, 68.3%-69.0%] and 71.3% [95% CI, 71.0%-71.6%] before and after the COURAGE trial, respectively;  $P < .001$  for difference between the periods).

### COMMENT

Our study demonstrated that less than half of patients undergoing PCI are taking OMT before their procedure, despite the guideline-based recommendations to maximize OMT and the clinical logic of doing so before PCI so that the need for additional symptom relief from revascularization can be appreciated. Even after publication of the COURAGE trial, little change in this practice pattern was observed. Although clinicians did increase the use of OMT before discharge, with antiplatelet agents being almost universally applied, almost a third of patients were not treated with OMT, a pattern that also did not change after the COURAGE trial was published. Collectively, these findings suggest a significant opportunity for improvement and a limited effect of an expensive,

highly publicized clinical trial on routine clinical practice.

Supporting the potential to improve treatment patterns, 79% of patients after receiving PCI in the COURAGE trial received the combination of aspirin,  $\beta$ -blockers, and statins at 5 years after randomization and 55% received the combination of aspirin,  $\beta$ -blockers, statins, and ACE inhibitors or ARB<sup>4</sup> compared with our finding of 66% and 46% being prescribed these therapies at the time of discharge from PCI. The COURAGE trial investigators recently described the differences between the OMT delivery in the trial and that which may be possible in routine practice, concluding that health system modifications are needed to achieve successful application of OMT in practice.<sup>20</sup>

Our study demonstrates that although the use of OMT increases before discharge after PCI, there remains an important opportunity to develop innovative strategies to increase medical therapy in the comprehensive care of patients undergoing PCI, both before and after the procedure. The responsibility of administering the full complement of medical therapy, however, ought not to be placed solely on the interventional cardiologist, but rather be a shared responsibility with the primary physicians caring for the patient.

Our findings suggest a promising possibility of developing better care through better collaboration. Although patients with stable CAD who are receiving PCI are often only in the hospital for less than 24 hours, multidisciplinary teams could use this time to optimize a patient's medical regimen, use the "teachable moment" of an invasive procedure to impart to patients the importance of medication adherence, and engage the patient in a program that supports the transition of care so that important medications are implemented.

Our study is congruent with and extends an extensive literature documenting suboptimal use of recommended preventative therapies.<sup>13,21-28</sup> Al-

though a single center study did show a small increase in the use of anti-ischemia medications and initial OMT strategies following the release of the COURAGE trial,<sup>29</sup> our results in a significantly larger national sample are more representative of current US practice.

In an era of increasing demand for comparative effectiveness studies, our findings highlight a challenge in translating the results of such studies to clinical practice. The purpose of the \$33.5 million COURAGE trial was to compare the effectiveness of 2 treatment strategies for patients with stable CAD. However, despite enrolling 2287 patients from 50 sites in the United States and Canada,<sup>30</sup> the virtually flat time-trends in our study show that the COURAGE trial results did little to change practice patterns of providing OMT for patients with stable CAD receiving PCI in the United States. Although other studies have shown a decrease in the use of PCI,<sup>31</sup> particularly for those patients with stable CAD,<sup>32</sup> suggesting that the COURAGE trial results are being applied before referral for PCI, our findings demonstrate a continued opportunity to improve care among those patients who do receive PCI. Although we observed small statistical increases in OMT after the COURAGE trial, these numeric increases are of marginal clinical significance and suggest that the field of comparative effectiveness research, being supported by the Patient Protection and Affordable Care Act with funding and establishment of the Patient-Centered Outcomes Research Institute,<sup>33</sup> will need to invest heavily in implementation research to facilitate the translation of evidence from "bench to behavior."<sup>34,35</sup>

There are several possible reasons why the COURAGE trial results may not have been incorporated into practice to the extent that might have been anticipated. First, the results of the trial were not universally accepted, due in part to the selected group of patients studied in the trial.<sup>36</sup> However, even if the COURAGE trial population repre-

sented a selected group of those patients undergoing PCI, there is no clinical logic to support that secondary prevention with aspirin,  $\beta$ -blockers, and statins among patients who are not eligible for the COURAGE trial would not be important in optimizing their long-term outcomes. Second, a continued knowledge gap may exist regarding the principal findings of the COURAGE trial. This seems unlikely, however, given the almost unprecedented publicity that surrounded the trial. Third, the generalized challenges of implementing both clinical trial data and practice guidelines into clinical use may have been a factor<sup>9-12,37,38</sup>; however, the use of antiplatelet therapy was successfully applied in virtually all patients. In addition, some physicians may believe that stents are better than medical therapy for patients with stable CAD, even in the absence of evidence to support this view.<sup>39</sup>

Our study identifies a promising opportunity to improve the quality of care for patients undergoing PCI. Given the scientific consensus on the importance of optimizing medical therapy in patients with CAD, regardless of whether revascularization is performed, it is logical to conclude that attempting OMT before PCI is important. Moreover, if the COURAGE trial study results were to be implemented in practice, a patient with stable CAD would have a diagnostic coronary angiogram and, if not receiving OMT, could defer PCI until OMT had been applied with continued symptoms. Because all of the patients in our study received PCI, rather than only diagnostic coronary angiograms, it is reasonable to assess for the degree of OMT before the procedure. Moreover, even among those patients with previously known cardiovascular disease, approximately half (46.4%) were not receiving OMT before PCI, despite having definite indications for aggressive secondary prevention. Not only can OMT minimize the risk of mortality in appropriate patients, but many patients with symptoms may no longer have those symptoms after OMT is initiated, thereby

decreasing the eventual need for revascularization. In the COURAGE trial, the quality of life benefit for OMT alone was 3 to 4 times greater than the incremental benefit of PCI over OMT.<sup>6</sup> From a societal perspective, aggressive use of OMT, including before PCI, offers the opportunity to both improve survival and decrease costs by potentially avoiding PCI in those patients who become asymptomatic after OMT alone. However, achievement of OMT in clinical practice is clearly a challenge.

Our study should be interpreted in the context of several potential limitations. First, because the study population is derived from a group of institutions who participate in the registry, it may reflect institutions that are more focused on evidence-based medicine. However, any selection bias from this would be expected to overestimate the application of OMT, suggesting that the findings may be conservative. Second, medication contraindications may be underdocumented in the registry, which could underestimate OMT rates. However, any underdocumentation of contraindications would not be expected to differ before and after the COURAGE trial, thus not altering the finding that rates of OMT were similar between periods. Third, some clinicians may have recommended the use of OMT to the referring physicians but not instituted the recommendations in the patients themselves. There is, however, a large body of literature showing that sustained use of medications is markedly higher among those patients who were discharged on these medications than those who were not.<sup>40-43</sup> For example, Butler et al<sup>41</sup> showed that  $\beta$ -blocker prescriptions at the time of hospital discharge after a myocardial infarction were associated with significantly higher 1-year adherence, underscoring the importance of actually prescribing rather than just recommending OMT. In addition, we evaluated a cohort of patients undergoing PCI. A higher proportion of patients with stable angina may have been treated with OMT alone after the publication of the COURAGE trial, but this

would not undermine the value of attempting OMT before PCI.

In conclusion, our study identifies an important opportunity to optimize medical therapy before and after PCI. Our study also highlights the modest changes in clinical practice after the publication of a large randomized controlled trial underscoring the importance of OMT in stable ischemic heart disease. These findings support a call for innovations in how OMT is incorporated into interventional strategies and for improving the translation of clinical evidence into practice.

**Author Contributions:** Dr Borden had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Study concept and design:** Borden, Redberg, Spertus.  
**Acquisition of data:** Borden, Redberg, Dai, Kaltenbach, Spertus.

**Analysis and interpretation of data:** Borden, Redberg, Mushlin, Spertus.

**Drafting of the manuscript:** Borden, Spertus.

**Critical revision of the manuscript for important intellectual content:** Borden, Redberg, Mushlin, Dai, Kaltenbach, Spertus.

**Statistical analysis:** Dai, Kaltenbach.

**Obtained funding:** Borden, Spertus.

**Administrative, technical, or material support:** Borden.  
**Study supervision:** Redberg, Mushlin, Spertus.

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